

L35 ANSWER 167 OF 272 HCAPLUS COPYRIGHT 2006 ACS on STN

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TITLE: Preparation of substrate-spacer-active substance
prodrugs

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PATENT ASSIGNEE(S): Behringwerke AG, Germany

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FAMILY ACC. NUM. COUNT: 2

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EP 647450	A1	19950412	EP 1993-114475	19930909
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
EP 595133	A2	19940504	EP 1993-116702	19931015
EP 595133	A3	19981104		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
IL 107398	A1	20010128	IL 1993-107398	19931025
CA 2109259	AA	19940428	CA 1993-2109259	19931026
CA 2109259	C	20050524		
NO 9303854	A	19940428	NO 1993-3854	19931026
NO 311830	B1	20020204		
AU 9350225	A1	19940512	AU 1993-50225	19931026
AU 669218	B2	19960530		
JP 06293665	A2	19941021	JP 1993-266976	19931026
ZA 9307951	A	19950705	ZA 1993-7951	19931026
US 5955100	A	19990921	US 1995-449021	19950524
US 6146658	A	20001114	US 1997-859084	19970520
PRIORITY APPLN. INFO.:			DE 1992-4236237	19921027
			US 1993-140825	A3 19931025
			US 1995-449021	A1 19950524

AB Compds. of the form substrate-spacer-active substance, where the substrate and spacer are cleaved under physiol. or pathophysiol. conditions, the substrate is not an amino acid or peptide residue, and the active ingredient is a chemical compound with biol. activity or a derivative thereof, with the exception of N-bonded derivs. of anthracycline, paranitroanilide, or cytosine arabinoside, were prepared Thus, 3'-N-fluorenylmethoxycarbonyldoxorubicin in PhMe was treated with diisopropylethylamine and diphosgene; after 1 h 4-(6-O-methyl- β -D-glucuronyloxy)-3-nitrobenzylamine and diisopropylethylamine in DMF were added and the mixture was stirred 14 h to give, after deprotection, 14-O-[4-(β -D-glucuronyloxy)-3-nitrobenzylaminocarbonyl]doxorubicin (I). I showed an acute LD50 in mice of >1500 mg/kg, vs. 20 mg/kg for doxorubicin itself. I at 500 mg/kg in mice implanted with human LOVO colon tumors showed a T/C = 40.0%.

IT 59865-13-3DP, Cyclosporin a, substrate-spacer prodrugs of

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

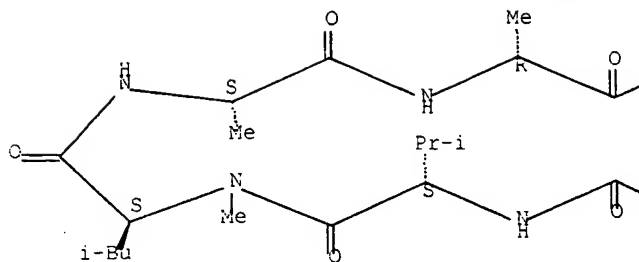
RN 59865-13-3 HCAPLUS

CN Cyclosporin A (9CI) (CA INDEX NAME)

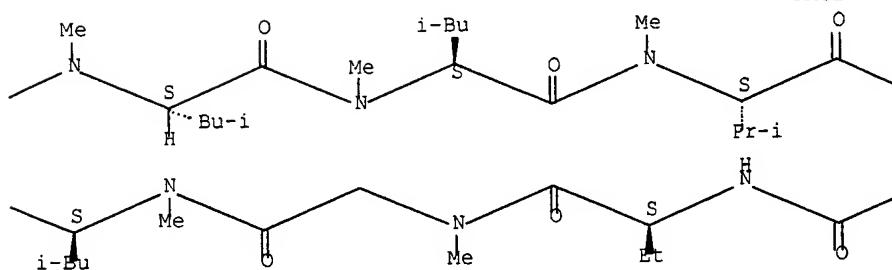
Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



PAGE 1-C

